

THE WORLD OF CHEMISTRY

Program #23

PROTEINS:
STRUCTURE AND FUNCTION

Producer Doug Bolin

Air Script: October 31, 1988

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Annenberg/CPB Project Logo and Music

Funder Credits

MONTAGE: Factory,
microscopic cells, people,
computer model

NARRATOR (MUSIC and NAT
SOUND under):

This enormous chemical factory labors
night and day producing many different
products. But a single microscopic cell
can perform much more varied
chemistry faster and more efficiently
than any chemical plant on this planet.
The chemistry of life. How do cells
perform the chemistry that makes life
possible? What is the secret? It is
hidden in a vital class of molecules:
proteins, and their structure and
function.

SUPER: PROTEINS:
Structure and Function

THE WORLD OF CHEMISTRY OPEN: Montage, Music, Logo

RH at sheep farm

ROALD HOFFMANN (SYNC):

People have been herding sheep since the early Stone Age, not only for their meat and milk, but primarily for their wool, the first natural fiber which humans made into a fabric. Wool is the fleece of sheep, and the fibers of wool are made up of molecules called proteins.

Proteins are there not only in wool but also in my hair, in my muscle, and that of the sheep. They are in my eyes receiving the light. They digest food. In general, they run the body.

MONTAGE: Wildlife, computer models, microscopic cells, wool, silk, hair, people

NARRATOR (MUSIC and NAT SOUND under):

Despite its diversity, all life on our planet shares one thing in common, compounds of carbon, and, most importantly, molecules of proteins. The story of life is the story of proteins, and the story of proteins is a story of structure and function. Proteins can do many things. They serve as structural materials. Wool, silk, hair, beaks and nails, all are made of protein molecules. Other proteins serve as enzymes, catalyzing reactions within living cells. Still others transport vital materials to the cell and, in turn, remove wastes. (cont.)

NARRATOR cont:

Hemoglobin, the molecule that transports oxygen in red blood cells, is a protein. Proteins catalyze and control the reactions that allow us to grow and keep us alive. They regulate body metabolism, store vital nutrients, and protect us from disease. We eat proteins; we wear proteins; we are proteins. The total number of different kinds of proteins in all species of living organisms is somewhere in the range of one-thousand billion, yet all proteins are composed of only 20 basic building blocks, called amino acids. How can such a fantastically huge number of different molecules arise from only 20 basic building blocks? The answer begins with a careful look at the structure of amino acids.

GRAPHIC: Amino acids

NARRATOR (MUSIC under):

Each amino acid has a common structure. A carbon atom is in the center. An amino group is attached on one side, and an acid group is attached on the other side. A hydrogen is also attached. A fourth group is called the side group. Each amino acid has a different type of side group. These are represented by different shapes. All amino acids but one are optically active chiral-molecules. In most living things, only one isomer exists.

Colored beads on a string

NARRATOR:

Amino acids link together like beads on a string to form the long sequences called polypeptide chains. The structure and function of a protein molecule is determined by the order, the number, and the kind of amino acids in the chain. This sequence of amino acids is called the primary structure. How does the chain form? How does polymerization take place?

GRAPHIC: Formation of a polypeptide chain

NARRATOR (MUSIC under):

Here is one amino acid with its side group, represented by the ellipsoid, and here a different amino acid with a different side group, represented by a hexagon. When the two amino acids are next to each other, the amino group of one can react with the acid group of the other. When this happens, water is eliminated and a peptide bond is formed.

Colored beads on a string

NARRATOR:

One by one, more amino acids are linked to form a long chain. Many proteins have more than a hundred amino acid units in a single polypeptide chain.

GRAPHIC: Amino acid chains,
computer models

NARRATOR (MUSIC under):

Each chain has a backbone composed of repeating units. Attached to this backbone are the different side groups. The optically active chains of amino acids are what makes life and its diversity possible. All life depends upon the arrangement of amino acids in the chain. Why? In the story of protein structure, the chain is merely the starting point. In reality, most chains are twisted and coiled. What accounts for this coiling? Hydrogen bonds. Hydrogen bonds between different portions of a single chain, or between chains, gives a second level of structure to proteins.

Weaving silk

NARRATOR (NAT SOUND under):

The different properties of hair, wool, and silk are determined by the structure of their protein molecules. Our present models of protein structure are derived from the study of x-ray diffraction patterns of crystallized proteins. Because of the complexity of protein structure, we only began to understand them in the middle of this century.

Archival footage of
Linus Pauling

NEWSREEL ANNOUNCER (VO):

In Stockholm, Sweden, the coveted
Nobel prizes. Honored for chemistry is
Dr. Linus Pauling of the California
Institute of Technology.

Archival footage and
photographs of Linus
Pauling, Linus Pauling at
work at home in Big Sur

NARRATOR (NAT SOUND under):

One of the key steps in unraveling the
mystery of hydrogen bonds in protein
structure involved this man, Linus
Pauling, a cold, and a Nobel prize. 1988.
Pauling lives in the Big Sur region of
Northern California. His living room is
his office. There he spends a large part
of each day at a simple desk, working on
a new research interest, metals. Earlier
in his career, Pauling had another
interest, the structure of protein
molecules. At that time there were
several conflicting theories. Pauling and
his colleagues thought that the first level
of protein structure was a polypeptide
chain. Then they asked themselves a
fundamental question.

INTERVIEW: Dr. Linus
Pauling

SUPER: Linus Pauling

DR. LINUS PAULING (SYNC):

We asked: How is the polypeptide chain folded? We couldn't answer the question, but we said it's probably held together by hydrogen bonds. The conclusion we reached was that there are -- that the pep -- polypeptide chains in the protein, which are far longer if they were stretched out than the diameter of the molecule, are coiled back and forth, and that they are coiled into a very well-defined structure, configuration, with the different parts of the chain held together by hydrogen bonds. In 1937, I spent a good bit of the summer with models for -- I assumed that I knew what a polypeptide chain looks like except for the way in which it's folded. And I wanted to fold it to form the hydrogen bonds. I didn't succeed. The fact is, I thought that there was something about proteins that perhaps I didn't know.

Archival photographs of
Linus Pauling

NARRATOR:

Pauling continued to work on this problem, but the solution eluded him. Then one day he had a crucial insight in a completely different and unexpected setting.

INTERVIEW: Dr. Linus
Pauling cont.

DR. LINUS PAULING (SYNC):

I had a cold. I was lying in bed for two or three days, and I read detective stories, light reading, and for awhile, and then I got sort of bored with that. So I said to my wife, "Bring me a sheet of paper, and I'm going to -- I think I'll work on that problem of how polypeptide chains are folded in proteins." So she brought me a sheet of paper and the slide rule and pencil, and I started working.

Polypeptide chain
on paper

NARRATOR (NAT SOUND under):

Using the knowledge gained from his years of model building, he drew the backbone of a polypeptide chain on a piece of paper. Then it occurred to him to try to fold the paper to see how hydrogen bonds could form along the polypeptide chain. The result was a structure that twisted around like a spring.

INTERVIEW: Dr. Linus
Pauling cont.

DR. LINUS PAULING (SYNC):

Well, I succeeded. It only took a couple of hours of work that day, March of 1948, for me to find the structure, called the alpha helix.

Archival photographs of
Linus Pauling

NARRATOR:

Pauling's insight was a huge stride towards understanding the structure of proteins and the role of hydrogen bonds in the second level of protein structure. For this work, he was awarded the Nobel prize in 1954.

GRAPHIC: Hydrogen bonding
to form the alpha helix

NARRATOR (MUSIC under):

How do these hydrogen bonds form? Here is a portion of a polypeptide chain. In order to reach its lowest energy state, the oxygen of a CO group forms a bond with the hydrogen of an NH group. Think of the chain as a ribbon, represented here by this green area. When the oxygen-to-hydrogen bond forms, it twists the ribbon around itself, forming a spring-like coil called the alpha helix.

Styling and modeling
hair

NARRATOR (MUSIC and NAT
SOUND under):

Human hair is an example of the alpha helix structure, and what is permanent waving? Refashioning proteins. Kitty Victor is International Director of Marketing for Redken. For the World of Chemistry, she is about to reveal the secrets of a permanent wave.

INTERVIEW: Kitty Victor,
International Director of
Marketing, Redken Inc.

SUPER: Kitty Victor

KITTY VICTOR (SYNC):

Basically, you'll be shampooing it,
rinsing it, putting a brush through it,
and going. That's all that you need to do
with it, all right?

WOMAN (SYNC):

Let's go.

KITTY VICTOR (SYNC):

Great. Let's get your shampoo.

Hair, spring

NARRATOR:

The alpha helix structure is what gives
hair its ability to stretch. Just like a
spring, the hair can be pulled into longer
shapes and then bounce back.

GRAPHIC: Hair structure

NARRATOR:

In hair protein, which is rich in sulfur,
each alpha helix coils around two other
alpha helices to form a rope-like
structure. These ropes form bundles,
held together by covalent sulfur-to-
sulfur bonds between side groups.

Applying permanent
solution

NARRATOR (NAT SOUND under):
During a permanent wave, hair stylists
use chemical solutions to first break, or
soften, these disulfide bonds and then
reform them. Dr. David Cannell, Chief
Research Chemist at Redken
Incorporated.

INTERVIEW: Dr. David
Cannell, Chief Research
Chemist, Redken Inc.

SUPER: David Cannell

DR. DAVID CANNELL (SYNC):
The disulfide bond is a chemical bond
formed from two sulfur atoms, fitting
this between protein chains or between
two different parts of the same chain.

INTERVIEW: Kitty
Victor cont.

KITTY VICTOR (SYNC):
What we're gonna do is, we want to
rearrange the bonds of the hair to
permanently curl them. By doing the
hair, or wrapping the hair around a rod
first, that's taking the formation that we
want the hair to be in. Then we will
apply the first solution that actually
softens the bonds and allows them to be
rearranged in a curly formation. In
actually, the bonds inside the hair are
lined up together. (cont.)

KITTY VICTOR cont:

Once we apply the solution, they start to break down or cleave these bonds, meaning that these disulfide bonds then take a new shape, they've actually moved down.

INTERVIEW: Dr. David Cannell cont.

DR. DAVID CANNELL (SYNC):

At the end of the waving process, the proteins that make up the hair structure have been sufficiently softened. They have moved internally with respect to one another to take on the shape of the permanent wave rod. We must now fix them in this new position, lock them in this new conformation, to impart a permanent wave to the hair. The waving solution is rinsed away and a neutralizer, or oxidizing solution is applied. However, the disulfide bond is not in the place it originally started. So, we're actually forming new disulfide bonds, which lock the hair in its new conformation.

INTERVIEW: Kitty Victor cont.

KITTY VICTOR (SYNC):

Kelly, I think you're gonna find this so easy to take care of. See what happens when you have your disulfide bonds broken?

WOMAN (SYNC):

It looks great.

MONTAGE: Silk

NARRATOR (MUSIC under):

Silk is an example of another type of structure formed by hydrogen bonds, the beta sheet. Silk's rare and prized properties are determined by the structure of its protein. This gives rise to silk's unusual strength and flexibility, and its one flaw. Unlike hair, silk doesn't stretch well.

GRAPHIC: Beta sheet formation

NARRATOR (MUSIC under):

In silk, the beta sheet structure is formed by hydrogen bonds between polypeptide chains. The process begins with a single polypeptide chain. As another chain approaches the first one, a large number of hydrogen bonds are formed between the chains, locking the chains strongly together. This is what accounts for the strength of silk. As more and more chains are locked into the beta sheet structure, it becomes very strong and flexible.

Silk, hair, wool, spring

NARRATOR (MUSIC under):

It's a very strong structure, but it is already stretched out and cannot stretch further without breaking. In contrast, the coiled alpha helix in fibers, such as human hair and sheep wool, allows the protein to stretch quite easily and then spring back.

RH in field

ROALD HOFFMANN (SYNC):

Wool, silk, hair, those are structural proteins. But this clever idea of nature's, to string together some amino acids to give function and variability, can be put to other purposes. In fact, the most important use of proteins is, as a resident chemists in the cell, to run an incredible variety of very specific chemical reactions, and to run them very, very efficiently.

MONTAGE: Chemical
plants

NARRATOR (NAT SOUND under):

Our huge industrial complex of chemical plants runs night and day carrying out chemical reactions. Yet, even a primitive cell is a biological chemistry factory that carries out hundreds of reactions in seconds, without high temperatures, without extreme pressures, with low amounts of energy and starting materials. A cell can produce an array of very complicated and pure compounds, each perfectly designed for a specific function. How does it do it?

Computer models

NARRATOR (MUSIC and NAT
SOUND under):

Through the use of enzymes. Enzymes.
The protein molecules that act as
enzymes are among the most complex
and important chemical creations in all
of nature. One of the tools that has
increased our understanding of enzyme
structure is found not on a laboratory
bench, but on a desk top, the computer.
Richard Feldmann is head of the
molecular graphics department at the
National Institutes of Health. He has
devoted much of his career to building
precise computer models of enzyme
molecules and other proteins, based on
X-ray crystallographic data.

INTERVIEW: Richard
Feldmann, head of the
molecular graphics
department, National
Institutes of Health

SUPER: Richard Feldmann

RICHARD FELDMANN (SYNC):
Proteins are exquisitely structured. And
if you change even one or two atoms in
a whole protein, the protein won't
function the way it should. And so we
want to understand how the protein is
structured. (cont.)

RICHARD FELDMANN cont:

We want to get a sense of how all the atoms really relate to each other, and we feel that once we do understand this, we'll know much more about how to correct molecules that are wrong, or how to design new molecules.

Computer models

NARRATOR (NAT SOUND under):

Here is a computer graphic of a small polypeptide hormone, glucagon, involved in sugar metabolism. One advantage of the graphics is that the hydrogens, and then the side groups, can be stripped away to reveal only the atoms in the polypeptide backbone. This compound's second level of structure is an alpha helix.

INTERVIEW: Richard
Feldmann cont.

RICHARD FELDMANN (SYNC):

Well, glucagon is just one helix. One can take a number of helices in an amino acid sequence and put them together. By taking a number of helices and putting them together in three-dimensional space, we can achieve a much more complex structure. Now, if these helices were strung out in a big string, then it would be a very curious and oddly shaped, sausage-shaped object. (cont.)

RICHARD FELDMANN cont:

What tends to happen, of course, is that the individual helices tend to pack together, and hence we get a globular shaped protein.

Computer models

NARRATOR (NAT SOUND under):

This is a model of myoglobin, found in muscle tissue. It has several sections of alpha helices, folded together to give a third level of protein structure, this compact globular shape.

INTERVIEW: Richard Feldmann cont.

RICHARD FELDMANN (SYNC):

From a display like this, we get some sense of the overall compact globular nature of the protein, and, in the case of this protein, there are only helices. In the other cases that we'll show will be a combination of helices and beta sheets. And those two features seem to make up most of the proteins that we've seen today.

Computer models

NARRATOR (NAT SOUND under):

This protein, flavodoxin, an enzyme found in nitrogen-fixing bacteria, has both alpha helices and beta sheet sections. In its tertiary structure, the beta sheets form a wall surrounded by helices.

INTERVIEW: Richard
Feldmann cont.

RICHARD FELDMANN (SYNC):

It's turned out that, as we looked at a variety of different proteins, that each protein has a particular way about it, that it folds up. And many of them are different. Some fold from the beginning towards the end, some fold from the middle towards the both ends, some fold one domain first and then another domain. And there's a whole bunch of different ways that proteins fold up. But sort of looking at each one, at least for me, gives some understanding about how they most probably fold up.

Computer models

NARRATOR (NAT SOUND under):

Before folding can occur, sections of the polypeptide chain have already formed alpha helices, shown in green. The non-helical blue portions of the chain will now come together to form the beta sheet structure. Gradually, the chain folds into the globular shape. This shape is further stabilized by several different types of bonds, some covalent, some ionic. These globular structures of enzymes govern the chemical reactivity of the cell.

INTERVIEW: Richard
Feldmann cont.

RICHARD FELDMANN (SYNC):
In a cell, there are lots of chemical reactions that have to, have to occur, and left to themselves, the small organic molecules, which just sort of wander around, occasionally bumping into each other, and the chemical reactions would be very slow. To make a cell work, you have to have these reactions occurring at steady and a faster rate. And so enzymes are used to make chemical reactions occur more specifically and faster.

Shots of supertankers

NARRATOR (NAT SOUND under):
If you can understand how a boat fits into a dock, you can understand how enzymes perform their catalytic action.

GRAPHIC: Simplified
animation of enzyme
action

NARRATOR (MUSIC under):
This shape represents the structure of the active site of the enzyme, or the dock. And this is a model of an optically active molecule the enzyme will act upon. It behaves like a very oddly shaped boat coming into a dock. Only one optical isomer will fit. The enzyme and this molecule are attracted to each other. (cont.)

NARRATOR cont:

But the molecule can only enter the enzyme in one way, so that each shape on the boat fits into the appropriate space in the enzyme dock. But as the molecule finds its place in the enzyme, something interesting begins to happen. Because of the way the atoms are arranged at particular points on the enzyme, one of the bonds is stretched and weakened. A new group moves in, bonds with the central atom, causing the already weakened bond to break. A new molecule, belonging to the same optical family, has been formed.

INTERVIEW: Richard
Feldmann cont.

RICHARD FELDMANN (SYNC):

The active site of the protein is formed by portions of the amino acid sequence all along the peptide chain, coming together in three dimensions. So there's not just any one piece of a polypeptide chain that's important. All of the amino acids along the chain are important. And the structure is important because it brings together all of these different amino acids and puts them in very specific spots in three dimensions, so as to control the chemistry that goes on.
(cont.)

RICHARD FELDMANN cont:

And that's the relationship, then, between the structure of the protein, the secondary features, the helix and the beta sheets, the amino acids that make them up, because those amino acids are projected into the active site and those amino acids do the chemistry which makes the enzyme work specifically and rapidly.

Heart attack victim,
ambulance, hospital
shots

NARRATOR (MUSIC and NAT
SOUND under):

Medical disorders can result from an overproduction of a certain chemical by the body. This can sometimes result from an enzyme that is too active. Using their knowledge of protein structure, scientists are now developing a new generation of drugs called enzyme blockers. Heart attacks rank as the number one cause of death in America. High blood pressure is a contributing factor to heart attacks, and, in some cases, is caused by the overactivity of an enzyme called rennin.

GRAPHIC: Heart and blood vessels

NARRATOR (MUSIC under):

Rennin is an enzyme that is involved in the production of the body's most powerful blood vessel constrictor. In cold weather, constriction of the blood vessels helps conserve the body's heat. But some individuals produce too much rennin too frequently, causing the blood vessels to be permanently constricted.

Heart attack victim, hospital shots, lab work

NARRATOR (NAT SOUND under):

The reduced size of the blood vessels leads to high blood pressure. A new drug that functions as a rennin blocker is now being developed to treat this condition by blocking the activity of the excess rennin.

GRAPHIC: Enzyme blocker mechanism

NARRATOR (MUSIC under):

Let's use our model enzyme to see how an enzyme blocker might work. Here on the left is the molecule on which the enzyme usually acts. The blocker molecule, on the right, is different in two respects. The blocker docks and forms a strong covalent bond with the enzyme. (cont.)

NARRATOR cont:

Since there is no mechanism for breaking this bond, the blocked enzyme can no longer play its role in producing the molecule that raises the blood pressure.

INTERVIEW: Richard Feldmann cont.

RICHARD FELDMANN (SYNC):

Is that it's very clear now that proteins, when they don't work right, cause diseases, and that the base of most of our diseases is some molecule, or molecules, that are not working the way they should, and that we can actually find detailed atomic reasons why something is not working the way it should.

SUPER: PROTEINS:
Structure and Function

MONTAGE: Program graphics,
colored beads on string,
computer models, hair

NARRATOR (MUSIC under):

To review: Proteins are large polymers built of amino acids. The number, kind, and sequence of amino acids in a polypeptide chain dictates all other levels of structure. This linear sequence is the primary structure of proteins. A second level of structure, the alpha helix and the beta sheet, is produced by hydrogen bonding. A third level of structure results from the folding of the secondary structure into a globular shape. (cont.)

NARRATOR cont:

Hair, wool, and silk are proteins with
only the first two levels of structure.

Enzymes are globular proteins that act
as catalysts.

Credits, Closing Montage, Closing Music

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